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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Caldwell et al.

Serial No.: 09/522,117

Group No.: 1624

Filed: March 9, 2000

Examiner: V. Balasubramanian

For: **COMPOUNDS CAPABLE OF ACTIVATING CHOLINERGIC RECEPTORS**

Date: February 28, 2001

BOX NON-FEE AMENDMENT

Commissioner for Patents

Washington, DC 20231

REQUEST FOR RECONSIDERATION

Dear Sirs:

This Request for Reconsideration is responsive to the Office Action of February 20, 2001. Claims 21-27 are currently pending.

I. § 103 Rejection

Claims 21-27 stand rejected under 35 U.S.C § 103(a) as being unpatentable over U.S. Patent No. 5,861,423 to Caldwell et al. The Action states, *inter alia*, that:

Caldwell et al. teaches several pyridinyl substituted olefinic amines claimed herein for central nervous disorders. . . . See example 4 on col. 16 which shows N-methyl-4-3-[5-isopropoxypyridinyl]-3-buten-1-amine.

While said compound doesn't anticipate the scope of claims 21-27, they are very closely related, being homologs of compounds i.e. instant pentene vs butene of the reference. However, homologs and compounds that differ only by a CH₂ are not deemed patentably distinct absent evidence of superior or unexpected properties. In re Wood 199 USPQ 137; In re Lohr 137 USPQ 548. Thus it would have been obvious to one skilled in the art at the time of the invention was made to expect instant compounds to possess the utility taught by the applied art in view of the close structural similarity outlined above.

Applicants respectfully traverse this rejection.

Applicants respectfully submit that the Action has failed to establish a *prima facie* case of obviousness. The Patent Office has the initial burden under §103 to establish a *prima facie* case of obviousness. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). A determination that an invention would have been obvious when it was made to someone of ordinary skill in the art under §103 is a conclusion of law based on fact. *Panduit Corp. v.*

Dennison Mfg. Co. 1 U.S.P.Q.2d 1593 (Fed. Cir. 1987), *cert. denied*, 107 S.Ct. 2187.

Applicants respectfully submit that the Patent Office has not made the requisite showing of fact to support the legal conclusion of obviousness.

A. The Action Has Not Established That the Claimed Compounds and the Reference Compounds Are Homologous

The Action alleges that in the art of amino alkenyl substituted 3-pyridinyl compounds with central nervous system activity “homologs and compounds that differ only by a CH₂ are not deemed patentably distinct absent evidence of superior or unexpected properties.” (Page 3). The Action has not shown, however, by evidence from the art of CNS-active compounds that one skilled in that art would find the two sets of compounds homologous, and would also reasonably expect similarity in their properties.

The mere fact that a claimed compound has an empirical formula that differs from the prior art compound by a CH₂ or a multiple thereof does not establish them as members of the same homologous series. *Ex parte Burtner* 121 U.S.P.Q. 345 (POBA 1951). In *Burtner*, the Board found that it was “evident from the standpoint of empirical formula [that] the esters of [the prior art] differ from those herein claimed by CH₂ or a multiple of CH₂.” 121 USPQ at 347. However, in reversing the Examiner’s finding of unpatentability over the prior art, the Board held that:

the critical question is not whether or not the alcohol moieties of the esters under consideration are to be considered homologous under some of the available definitions of that term, but whether or not the alcohols are sufficiently similar from the standpoint of structural chemistry so that those now claimed would be suggested to chemists from those disclosed and would be expected to have like properties.

Id. Similarly, in the case *Ex Parte Thompson*, 119 U.S.P.Q. 254 (POBA 1954), the Board noted that a comparison between the claimed compounds and the prior art compounds showed that the two sets of compounds were structurally related (claimed compounds required three methylene groups between two oxygen atoms, where prior art compound showed two methylene groups between two oxygen atoms). 119 USPQ at 255. In spite of this structural similarity, however, the Board reversed the Examiner’s finding of

unpatentability, holding that “no authority has been cited by the examiner leading to the conclusion that such relationship was one recognized by chemists as leading to equivalent or similar products.” *Id.* *Burtner* and *Thompson* thus both illustrate the legal principle that the allegation of similarity between a claimed compound and a prior art compound based merely on structural differences is not sufficient to establish homology, much less obviousness. Rather, there must also be a showing that one skilled in the art would have recognized the structural similarity as necessarily imparting similar properties. Applicants respectfully submit that the Action has not established that, in the chemical art of aminoalkenyl substituted 3-pyridinyl compounds useful in treating CNS disorders, one skilled in the art would have recognized that the presence of an alkyl substituent in the place of a hydrogen substituent on the alkenyl moiety as necessarily imparting similar properties.

In fact, Applicants note that the Board of Patent Appeals and Interferences (the Board) has held that compounds that might, at first blush, seem homologous to prior art compounds were patentable in view of the low predictability of activity in the CNS-active compound art. In the case *Ex parte Koo*, 150 U.S.P.Q. 131 (POBA 1965), the Examiner had initially found a claimed compound having CNS depressant activity unpatentable because it differed structurally from a prior art reference compound by a pyridinyl substituent instead of a phenyl substituent. The Examiner had supported the finding with secondary references stating that phenyl and pyridinyl compounds had been recognized as “equivalent bioisosteres.” Notwithstanding the secondary references indicating the general similarity between benzene, pyridine and their simple derivatives, the Board reversed the Examiner’s decision and held the claimed compounds patentable, stating that “considering that there is little predictability in this art,” the effect of the interchange between the two structurally similar groups “could hardly be foretold.” *Koo*, 150 U.S.P.Q. at 132. Applicants respectfully submit that the Action has not established that, in the chemical art of aminoalkenyl substituted 3-pyridinyl compounds useful in treating CNS disorders, the presence of an alkyl substituent in the place of a hydrogen substituent on the alkenyl moiety necessarily means that compounds are homologous.

B. The Determination of Homology Does Not Dictate a Finding of Obviousness

Even assuming that one skilled in the art would deem the claimed compounds and the reference compounds to be homologous, the determination of homology does not dictate a finding of obviousness. Homology is nothing more than a fact that must be considered with all other relevant facts in applying the statutory tests of obviousness. *In re Mills* 126 U.S.P.Q. 513 (CCPA 1960). Moreover, homology should not automatically be equated with *prima facie* obviousness; rather, 35 U.S.C. §103 requires that obviousness of invention as a whole must be shown. *In re Langer et al.*, 175 U.S.P.Q. 169 (CCPA 1972). As the Court stated in *Langer*,

[s]o it is that while this court has found the prior art disclosure of homologues of compounds to render *prima facie* obvious claims to those compounds, homology should not be automatically equated with *prima facie* obviousness.

Langer, 175 U.S.P.Q. at 171 (citations omitted). The Court was also careful to remark that although it had, in the past, made determinations of obviousness because homology between claimed compounds and prior art compounds had been established, the concept of having to show obviousness of the invention as a whole in view of the prior art as a whole "supercedes 'rules' which might emerge from the repeated application of other principles which may ordinarily be correct but fail under a set of facts which bring such principles in conflict with the broader notions of §103." *Langer*, 175 U.S.P.Q. at 171. Applicants respectfully submit that the Action has sought to apply a "rule" concerning homology to the pending claims, without establishing the factual basis for obviousness that 35 U.S.C. §103 requires. The Action appears to have alleged that homology necessarily equals obviousness. Applicants respectfully submit that homology is merely one of the many facts to be considered when reaching the legal conclusion of obviousness or non-obviousness.

C. The Claimed Compounds Show Unexpected and/or Superior Results Over the Reference Compounds

Even if one were to assume that homology between the claimed compounds and the reference compounds had been established, and further assume that this fact alone supported

a conclusion that the claimed compounds are *prima facie* obvious, absent a showing of unexpected results, Applicants still respectfully submit that the claimed compounds are not obvious in view Caldwell because the claimed compounds do, in fact, provide unexpected and/or superior results. Comparing a compound of the present invention, namely (4E)-N-methyl-4-[5-isopropoxy-3-pyridyl]-4-penten-2-amine¹, with a compound proposed by Caldwell, namely (E)-N-methyl-4-[3-(5-isopropoxypyridin)yl]-3-buten-1-amine², one finds that the difference between these two compounds is the presence of a methyl group on the alkenyl bridge connecting the amine moiety to the pyridinyl moiety of the compound of the present invention. Despite differing by one methyl group, these two compounds show different CNS activities. For example, the compound of the present invention provides an EC50 for dopamine release of 100, which is nearly 2 times greater than that provided by the Caldwell compound. As another example, the compound of the present invention provides a Ki of 10, which is nearly 2 times greater than that provided by the Caldwell compound. Applicants respectfully submit that the claimed compounds do, in fact, provide superior and/or unexpected results, and, thus, are not obvious in view of Caldwell.

For at least the foregoing reasons, Applicants respectfully request that these rejections be withdrawn.

II. Provisional Double Patenting Rejections

Claims 21-27 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 09/631,761.³ Claims 21-27 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 09/570,226. Applicants appreciate being made aware of the potential double patenting problem that may arise if one of the applications became a patent.

¹Page 30 of the instant application, Example 10, Sample 4.

²Caldwell, Column 16, Line 40-Column 17, Line 47 (Sample No. 4, Example 4,) and Column 22, Table I.

³Applicants respectfully submit that Application 09/631,761 was cited in error as this is not a copending application of Applicants. Applicants respectfully submit that the Action may have intended to cite Application 08/631,761, which is a copending Application of Applicants.

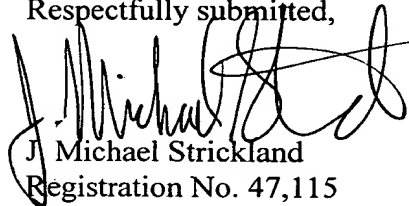
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Applicants respectfully request that these rejections be withdrawn and the present application allowed to issue as a patent. MPEP § 804 (I)(B).

III. Conclusion

The concerns of the Action addressed in full, Applicants respectfully request that the present rejections be withdrawn and that a Notice of Allowance be issued forthwith.

Respectfully submitted,




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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: BOX NON-FEE AMENDMENT, Commissioner for Patents, Washington, DC 20231, on February 28, 2001.



Monica Lago
Date of Signature: February 28, 2001